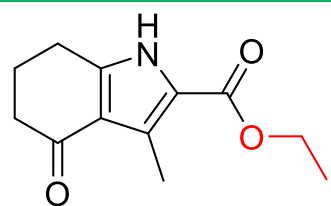


# **CNP27: SARS-CoV-2-NSP14 target-146 compounds (Nick Heaton library) HTS**



**Hadia Almahli**  
**28<sup>th</sup> Feb 2025**

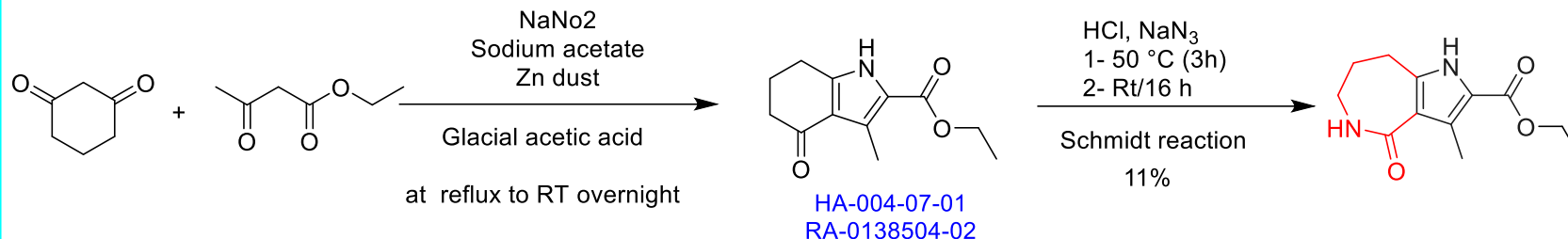
# CNP27: SARS-CoV-2-NSP14 target-146 compounds (Nick Heaton library) HTS



RA-0138504

MCULE-2755644375

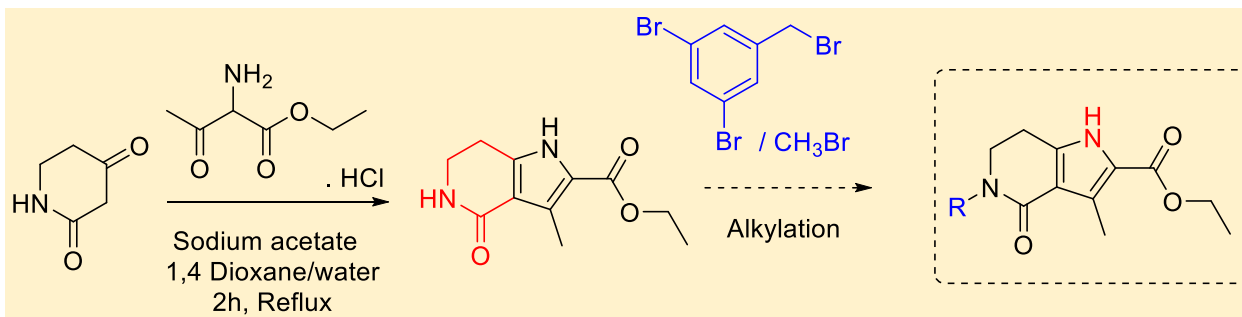
IC50 = 2  $\mu$ M



❖ Challenging work up & purification

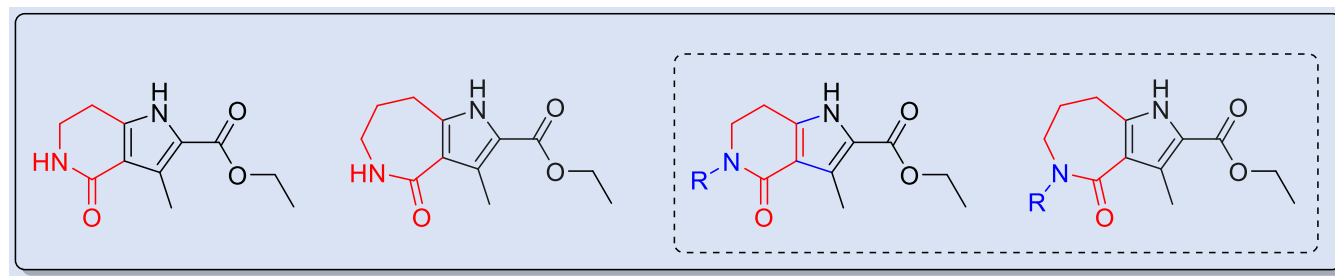


Weak yield

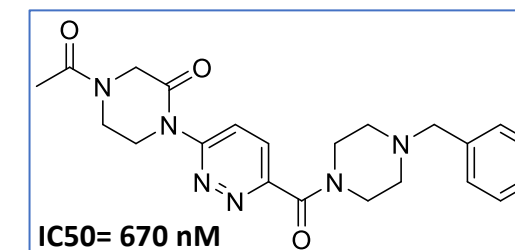
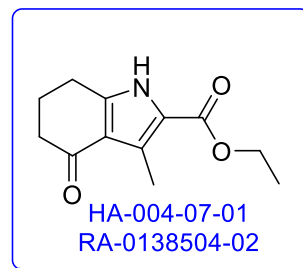
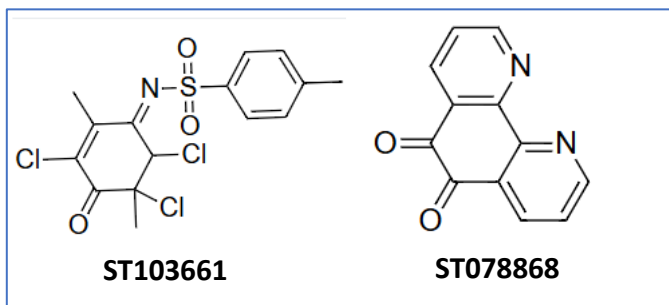


## Next plan:

- ❖ Piramal to make the lactams
- ❖ Alkylation
- ❖ Investigation of which N is alkylated



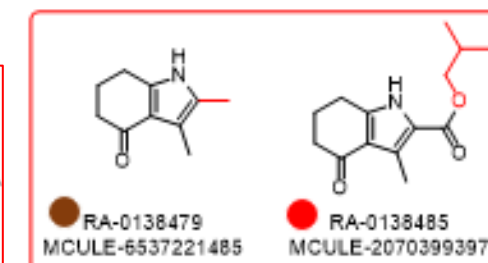
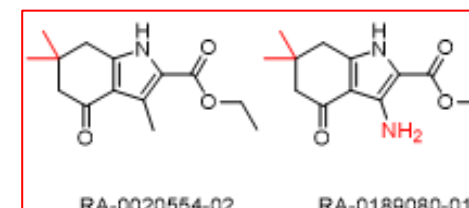
# CNP27: SARS-CoV-2-NSP14 target-146 compounds (Nick Heaton library) HTS



**Dual inhibitor  
MTase and ExoN inhibitor**

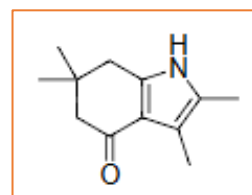
1.A High-Throughput Screening Pipeline to Identify Methyltransferase and Exonuclease Inhibitors of SARS-CoV-2 NSP14,  
*Biochemistry* 2025 64 (2), 419-431, DOI: 10.1021/acs.biochem.4c00490

- ❑ 22 Purchased and synthetic analogues of RA-0138504-02: to be tested by Joe Newman/the crystallized NSP10/14 protein by Vito
- ❑ Positive control if it's commercially available (ChemDiv-San Diego)
- ❑ Vero assay showed ST103661 and ST078868 as most potent hits

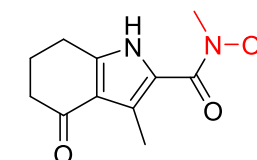
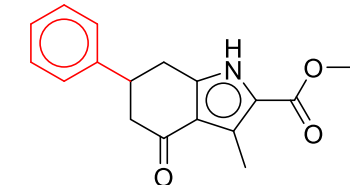
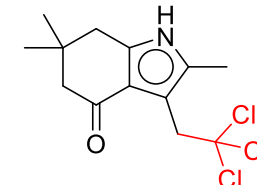
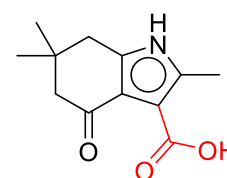
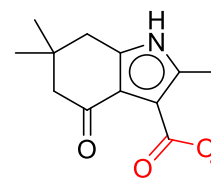
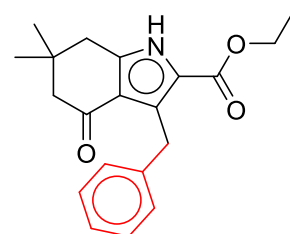


**Negative candidates**

## Craig-FRET ASSAY



RA-0020555-01



**Ordered from Molport**

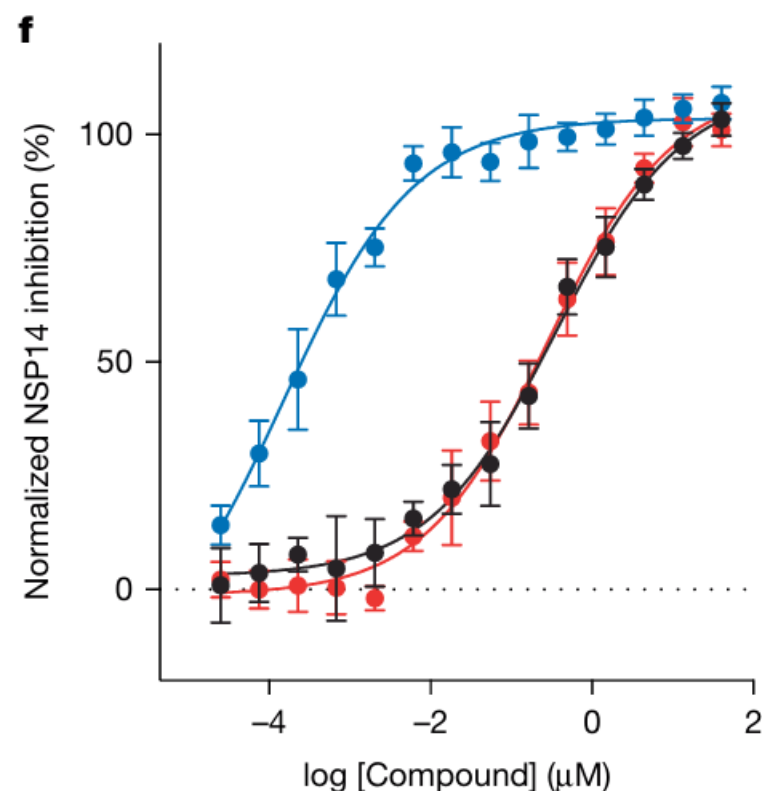
# CNP27: SARS-CoV-2-NSP14 target-146 compounds (Nick Heaton library) HTS



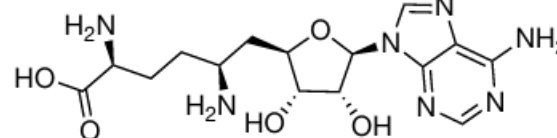
## Potent NSP14 inhibitors: Positive control MTransferase

Small-molecule inhibition of SARS-CoV-2 NSP14 RNA cap  
methyltransferase

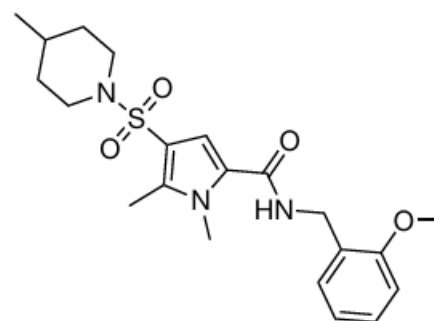
<https://doi.org/10.1038/s41586-024-08320-0>



● Sinefungin ( $\text{IC}_{50} = 285 \text{ nM}$ )



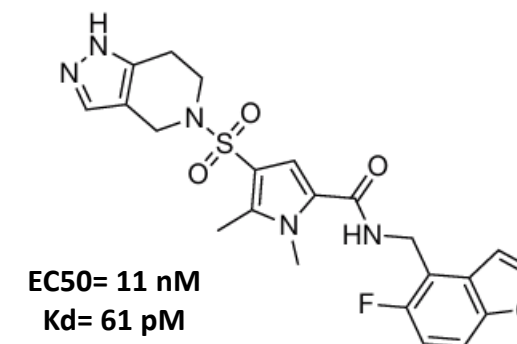
● RU-0415529 ( $\text{IC}_{50} = 356 \text{ nM}$ )



CAS No. : [3052313-73-9](#)



● TDI-015051 ( $\text{IC}_{50} \leq 0.15 \text{ nM}$ )



$\text{EC}_{50} = 11 \text{ nM}$   
 $\text{Kd} = 61 \text{ pM}$